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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,027	03/26/2002	William E. Jack	NEB-166-PUS	9409

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,027	JACK ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-42* is/are rejected.

7)☒ Claim(s) *43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Claims 32-43 remain pending and at issue for examination.

Applicant's election of the species of SEQ ID NO: 5, in the paper of 2/11/2008, is acknowledged.

Applicants' arguments filed on 10/31/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 43 objected to because of the following informalities:

Claims 43 is dependent on rejected claims 32 and 33. Applicant's comments regarding this objection are noted.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 32-42 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 32-42 are indefinite in that the metes and bounds of the claimed genus of methods is unclear and confusing given applicants recitation of "providing a DNA polymerase having an amino acid sequence that shows at least 30% overall identity with that of SEQ ID NO: 4…" The basis of this confusion is that SEQ ID NO: 4 is a 5837 nucleotide sequence. Since the claims are referring to "an amino acid sequence", it is unclear as to the relationship of the referred to amino acid sequence to the recited nucleic acid sequence. As their exist many potential ways to relate an amino acid sequence to a nucleic acid sequence, applicants intent is unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection is stated in the previous office action as it applied to previous claims 2-4, 14-17, 19-22 and 27-31. In response to this rejection applicants have cancelled all claims and added new claims 32-43 and traverse the rejection as it applies to the newly amended claims.

Applicants continue to traverse the current rejection on the same basis that they have previously argued, that of the decision in Invitrogen Corp v. Clontech Labs 77 USPQ2d 1161 (Fed Cir 2005) supports applicants position that the current claims satisfy the description requirement.

Applicants summarize the claim at issue of the *Invitrogen* case, as being drawn to a polypeptide having DNA polymerase activity and substantially reduced RNAse H activity, wherein said polypeptide is encoded by a modified reverse transcriptase nucleotide sequence that encodes a modified amino acid sequence resulting in said polypeptide having substantially reduced RNase H activity, and wherein said nucleotide sequence is derived from an organism selected from the groups consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents.

Applicants submit that the contrary to above, the pending claims include an *explicit* recitation of structural features (overall homology plus presence of a particular motif linked to the relevant activity) and that the present specification includes not one (as was the case in *Invitrogen)* but *six* examples of different DNA polymerases that fall within the scope of the claims used in the methods of the claims. Applicant also points out that: (1) at the time of the invention, the sequences of many DNA polymerase genes were known, (2) members of the DNA polymerase gene family share significant

homologies from one species to another, (3) the written description in the present case teaches that the invention can be applied to DNA polymerases other than the ones specifically exemplified and (4) the specification cites references providing the known sequences of such other DNA polymerases .

Thus, applicants submit that with regard to every relevant fact relied upon by the court, the present case has at least as much, and in many cases *more* description than was present in *Invitrogen.* This description supports a claim that itself includes *more precision* than was present in *Invitrogen.*

Applicant has also point to the written description guidelines and Example 14. Applicant submit that every DNA polymerase tested that has the recited structural characteristics has the recited activity and the Examiner has not provided any reason to doubt that other DNA polymerases with the recited characteristics would not also have this activity.

For all of these reasons, it is clear that the present claims meet the Written Description requirement.

Applicant's continued arguments regarding the *Invitrogen* case are acknowledged, however, applicants are again reminded that this case is based upon a different specification, different art, and different claimed subject matter and the merits of the instant specification must be based upon the current application. Unlike the *Invitrogen* case, the instant claims are not drawn to a polypeptide product, but rather they are drawn to a method of use of a very broad subgenus of DNA polymerases.

Said subgenus of DNA Polymerases must be capable of incorporating acyclonucleotides into a primer extension reaction. While applicants have presented six examples of encompassed DNA polymerases, and required the inclusion of a 15-amino acid motif, it remains that applicants have not related the subgenus of structure to the acyclonucleotide incorporation function.

While applicants comments regarding the homogeneity shared between this group of polymerases continues to be acknowledged, such is acknowledged in light of the degree of the vast majority of DNA polymerases, many of which have a high degree of homogeneity and not all of which share the ability to incorporate acyclonucleotides into a DNA fragment. Thus applicants reasoning that the degree of homogeneity between these polymerases would or should afford certain polymerase properties continues to not be persuasive.

It is this structure to function relationship that would help applicants in the description and enablement of the claimed genus. Applicants pointing out of the structure to function relationship of the archaeon Family B DNA polymerases, particularly SEQ ID NO: 4, with respect to general polymerase function continues to be acknowledged, however, not considered sufficient to describe those polymerases that have the necessary function of incorporating acyclonucleotides into a DNA fragment.

With respect to applicants assertion that applicants recited claims are analogous to the claims of example 14 of the Patent Offices Written Description Guidelines, applicants are reminded that these are in fact just that, guidelines, to be used to help one determine whether the claims in question meet the description

requirements. In using these guidelines one must look at all aspects of the claimed invention, not only those aspects raised by applicants, i.e. whether structural and functional limitations exist for the claimed genus, but also specifics of the recited structural and functional limitations and the relationship and interaction between the recited structure and the recited function and how this relates to the claimed genus.

Applicants complete argument continues to be recognized, but not found persuasive because just because applicants are limiting the claimed methods to methods of use of DNA polymerases which have a specific function, does not relieve applicants of the need to describe the claimed genus. This continues to be critical in light of the specific function recited and its relevance or association with the larger structural genus of DNA polymerases which do not have such a function.

Thus for the reason previously made of record and repeated herein applicants arguments continue to be found nonpersuasive.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 32-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method comprising providing a DNA Polymerase selected from the group consisting of Vent, Deep Vent, *Pfu* and 9°NTM or the specifically disclosed variants referred to in claim 43, with a template, a primer that binds to the template and a nucleotide solution containing at least one acyclonucleotide

and incubating the DNA polymerase with the template and the nucleotides so that the DNA polymerase extends the primer by incorporating the nucleotides, does not reasonably provide enablement for any method comprising providing a DNA Polymerase having an amino acid sequence that shows a mere 30% overall identity with that of SEQ ID NO: 4 (see also above rejection under 35 USC 112 second paragraph) and further includes a 15 amino-acid motif that is identical to SEQ ID NO: 5 except that it contains up to 3 amino acid substitutions as compared with the SEQ ID NO, with a template, a primer that binds to the template and a nucleotide solution containing at least one acyclonucleotide and incubating the DNA polymerase with the template and the nucleotides so that the DNA polymerase extends the primer by incorporating the nucleotides The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is stated in the previous office action as it applied to previous claims 2-4, 14-17, 19-22 and 27-31. In response to this rejection applicants have cancelled all claims and added new claims 32-43 and traverse the rejection as it applies to the newly amended claims.

Applicants have noted that the previous rejection of claims 2-4, 14-17, 19-22 and 27-31 is mooted by their cancellation and provided applicants reasons as to why the newly added claims should not be rejected on a similar basis.

Applicants continue to traverse the rejection by reiterating the arguments presented above relating to the written description requirement in their entirety as they relate to the enablement determination.

In so doing, applicants continue to go through the Wands factors below, in support of applicant's position. With respect to Factor (4) Nature of the Invention and (8) Breadth of the Claims: Applicant continues to argue that DNA extension reactions are well within the skill of those of ordinary skill, and the Examiner has argued that incorporation of acyclonucleotides may not be. Applicant submits that the *invention* is not the extension reaction, but rather the discovery that archeaon DNA B polymerases can incorporate acyclonucleotides, and indeed can incorporate them preferentially. Applicants argue that having established that they can, and further having shown that *six different such DNA polymerases* all can, Applicants have taught those skilled in the art that other polymerases of the class are likely also to have that activity.

Applicants submit that with respect to Factor (5) State of the Prior Art and (7) Predictability of the Art, the applicant and Examiner are in agreement that the prior art with regard to DNA polymerases and their classifications is extensive, however, applicants correctly note that the Examiner questions the "predictability of the art.., as to the basis of those claimed archaeon DNA polymerases that are able to incorporate acyclonucleotides". Applicant agrees that the prior art itself does not contain such predictions. However, applicants suggest that given that the prior art establishes the family of DNA polymerases and the present invention establishes that *all members tested* have the activity, Applicant respectfully submits that the claims are enabled.

Applicants submit that with respect to Factor (1) Quantity of Experimentation Necessary; (2) Amount of Direction or Guidance; and (3) Presence or Absence of Working Examples: The Examiner does not challenge that one of ordinary skill could make and test all polypeptides within the scope of the claim to determine their ability to extend a DNA primer or incorporate acyclonucleotides (including to determine their ability to preferentially select acyclonucleotides as compared with alternatives). However, the Examiner maintained with regard to the previously pending claims that "it remains that [Applicants] have not enabled one of ordinary skill in the art to make and use those [DNA polymerases] having the necessary acyclonucleotide incorporation properties". Applicants submit that this accusation is merely a statement of a conclusion and the Examiner has not articulated why the existing description and evidence provided might be insufficient; nor has the Examiner identified any particular information or evidence that Applicant would need to provide in order to satisfy the enablement requirement in the Examiner's view. This notwithstanding, Applicant respectfully submits that the present claims, which explicitly recite a key sequence motif as well as an overall degree of identity (thereby setting a boundary defining how closely related relevant polymerases must be to those whose activity.

For all of these reasons, Applicant respectfully submits that the present claims meet the enablement requirement.

Applicant's complete argument continues to be acknowledged and has again been carefully considered, however is not found persuasive on for the reasons previously made of record with respect to the previous claims set and repeated herein.

It continues to be acknowledged that the nature of the invention, the synthesis of a DNA, is well within the ordinary skill in the art, however, the incorporation of acyclonucleotides into a DNA or rather those polymerases which are capable of such incorporation is not as equally within the ordinary artisans skill. It continues to be realized that the pending claims are not directed to the use of any polymerase, but rather to a subgenus of polymerases that have a specific function for which insufficient guidance is provided and the breadth of encompassed polymerases encompassed by the claimed methods continues to be excessive.

The examiner continues to acknowledge the state of the art, and continues to emphasize that with respect to the predictability of the art, it continues to be questioned as to the basis of those claimed archaeon DNA polymerases that are able to incorporate acyclonucleotides into a DNA relative to the broadly claimed structural genus of DNA polymerase. Applicants have disclosed this specialized property in six DNA polymerases. In spite of applicants previous and above assertions it continues that applicants have not disclosed any structure and function relationship responsible for this specialized polymerase function.

Applicants newly added claims are acknowledged as well as applicants recitation that the claimed genus of DNA polymerases must have an amino acid sequence identity that shows a mere 30% overall identity with that of the nucleic acid of SEQ ID NO: 4 (see above rejection under 112 second paragraph) and further includes a 15 amino acid motif related to SEQ ID NO: 5-22. The claimed genus of methods of use of this genus of DNA polymerases continues to be excessive and it continues as to

how this single motif recited in the claims is related to the apparent specialized function of this class of DNA polymerases.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the claimed methods of use of those recited DNA polymerases with the specified acyclonucleotide incorporation characteristic. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those methods and polymerases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rgh
5/23/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652